

Abstract of the Invention

5 The present invention is a model for a mutually exclusive domain
folding molecular switch comprising a two-domain, bifunctional fusion protein
wherein the free energy released by the folding of a first domain of the fusion protein
drives an unfolding of a second domain of the fusion protein, and vice versa. The
molecular structure of the fusion protein is engineered so that, at any time, the folding
10 of the first domain necessarily unfolds the other domain, and vice versa, thereby
making the folded and unfolded states of the first and second domains mutually
exclusive. This is accomplished by the insertion of an exemplary insert protein into a
surface loop of an exemplary target protein subject to a novel structural design
criterion wherein the N-C terminal length of the exemplary insert protein is at least
15 two-times greater than the C α -C α length of the surface loop of the exemplary target
protein.